Our ref: KON-1870 Client's ref: P6388-001-0000 (US)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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In re Application of: Eiichi UEDA, et al : Art Unit: 1618

Appln. No.: 10/824,095 : Examiner: M.J. Perreira

Filed: April 13, 2004 :

For: LIPOSOME-CONTAINING RADIOGRAPHIC CONTRAST MEDIUM AND PREPARATION METHOD THEREOF :

CONFIRMATION #6153

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DECLARATION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

S i r:

I, Eiichi UEDA, hereby declare and says as follows:

1. I am one of the Inventors in this Application.

2. I received a Masters Degree in Chemistry from Tokyo University of Science in March of 1983. Since April of 1983, I was employed by Konica Corporation, the predecessor in interest to the current Assignee, Konica Minolta Medical & Graphic, Inc. Since my initial employment with Konica, I have been engaged in research and development in the field of material science to include radiographic contrast mediums.

3. I am aware that the Examiner has cited U.S. Patent 4,192,859, Mackaness, and U.S. Patent 5,676,928, Klaveness, as teaching a radiographic contrast medium comprising liposomes which are in the form of vesicles and including a water soluble non-ionic iodine compound, where the contrast medium contains substantially no chlorine solvent. In order to demonstrate the difference between the teachings of Mackaness and Klaveness, the contrast medium of Mackaness and Klaveness have been made and tested. The tests results are reported herein. These tests were performed by me or under my direct supervision and control.

4. In order to make the material of Mackaness, Example 1, as taught in Column 4, line 59 through Column 5, line 3, was followed. In order to make the material of Klaveness, the material of Example 1 at Column 12, line 11 through line 30, was performed. These contrast mediums obtained from both Example 1 of Mackeness and Example 1 of Klaveness was then tested for the amount of chlorinated solvent in the contrast medium and to determine whether the liposome was unilameller vesicle.

5. The determination of chlorine solvent in the contrast medium was measured using a gas chromatograph mass spectrometer model 5890 Series II / 5971 manufactured by Hewlett Packard. The internal standard compound was a fluorobenzene solution. The column was a HP-624 with an ID of 0.25 mm and a length of 30 m.

6. For the contrast medium of Mackaness, the amount of chlorinated solvent that remained in the contrast medium was 500 µg per liter. For the contrast medium of Klaveness, the amount of chlorinated solvent that remained in the contrast medium was 80 µg per liter. I note that the term "substantially no chlorine solvent", as used on page 27 of the Application, means that the contrast medium

contains chlorine solvent in an amount of not more than 10 µg per liter of contrast medium. Both the contrast medium of Mackaness and the contrast medium of Klaveness exceeded the limitation of "substantially no chlorine solvent".

7. The form of the liposome was tested using a transmission electro microscope as taught in the Application in the paragraph bridging pages 27 and 28 and in the paragraph bridging pages 42 and 43 of the Application. The liposome of Mackaness did not result in a substantially unilamellar vesicles. It was also noted that the liposome of Klaveness did not result in substantially unilamellar vesicles. In other words, the vesicles of Mackaness and Klaveness was not a single phospholipid bilayer.

8. I have reviewed the teachings in both Mackaness and Klaveness and am of the opinion that neither Mackaness nor Klaveness teach making a liposome which is comprised of vesicles including a water soluble non-ionic iodine compound wherein the liposome is substantially a unilamellar vesicle.

9. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 USC 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Eiichi Ueda

Eiichi UEDA

Dated: This 28th day of December, 2006.

DCL/mr